

of water, which, after standing from a half to one hour, were introduced in portions of 1 cm.³ into four series of test-tubes containing 90 mgrm. of maltose dissolved in 4 cm.³ of water. The concentration of the substrate in this experiment is $M/20$, while the enzyme concentration varies between 2×10^{-4} and 20×10^{-4} grm. per cm.³. After 16 hours' incubation, the action was stopped, and the quantity of maltose hydrolysed in each tube was determined as before. The numbers obtained are set out in Table III.

On plotting the percentage of maltose hydrolysed against the mean temperature of the experiment the curves of fig. 2 are obtained.

Here, again, each curve shows a maximum in the same region of temperature, $+47^{\circ}$. Consequently, the optimum temperature of the enzyme is independent of the enzyme concentration.

Thus it is found, for the *maltase* of *Aspergillus oryzae*—as for the *salicinase* of sweet almonds—that the optimum temperature of the ferment is independent alike of the concentration of the substrate and of the concentration of the enzyme.

A Theory of the Action of Rays on Growing Cells.

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The recent accessions to our knowledge of the nature of γ - and X-rays bring the treatment, by these rays, of malignant and morbid growths, into continuity with the treatment of lupus, etc., by the Finsen light or by other actinic radiation.

The pathological effects of the shorter and more penetrating waves have been described by experienced observers as stimulative of the morbid growth when the administered radiation is feeble in intensity and as inhibitive of growth when the radiation is sufficiently intense. Here there is plainly an effect produced by the short waves upon the growing cell, and the question arises if from this and allied observations we cannot gain some insight into the nature of the activity which characterises the malignant and morbid cell.

The well ascertained facts of photo-electricity show that, in all cases, the phenomena of direct light effects classed under that head are ascribable to the expulsion of electrons as a result of the vibratory energy communicated from the ether. The loss of electrons is attended by ionisation of the atomic or molecular systems from which they are derived, the abstraction of the

negative charge leaving the positively electrified ion behind it. This is the sufficient explanation of many phenomena collected under the name of photo-electricity. It has been ascertained that the velocity of the electron at the moment of its expulsion is the greater the shorter the wave-length of the radiation concerned. The swift-moving β -rays represent the electronic discharge excited by γ - and X-radiations.

Some years ago I endeavoured to explain the nature of the events taking place in the photographic film in terms of photo-electric activity. The theory has recently been republished and amplified by Mr. H. Stanly Allen in his book on photo-electricity.

According to my view the latent image is formed of molecular systems which have been subjected to loss of electrons and which remain as ions positively charged in presence of these electrons, the nature of the medium being responsible for the maintenance of the static attraction between electron and ion. In development these ions and electrons are discharged, and as a consequence of the chemical reaction thereby effected between the developer and the ionised photo-system the metallic atom is liberated, constituting the visible image. The phenomenon of the reversal of the latent image under excessive light stimulus is well known. On the theory this significant event is explained as the result of the increasing electrostatic stress attending over-exposure, whereby ultimately the resistance to recombination breaks down and the original molecular structure is restored. The luminous stimulant will now begin to re-form the latent image. A succession of such constructive and destructive effects is obviously possible according to the theory, and is, in fact, matter of observation. The theory can be shown to explain the facts respecting the different types of reversal as ascertained by R. W. Wood. Classifying the modes of formation of the latent image as (1) by pressure, (2) by X-rays, (3) by light-shock (very brief flashes, as by light from an electric spark), (4) by lamp light, Wood found that the latent impression produced by any one of these can be reversed by subsequent exposure to any other following it on the list but not by any one preceding it. He found that Becquerel rays (γ -rays) behaved like X-rays. For the manner in which Mr. Allen applies the photo-electric theory to these observations I refer to his book.

My object in referring to the photo-electric theory of photographic actions is to show that on the assumption that growth in the cell, generally, is attended and conditioned by ionic activity, there is sufficient resemblance between the effects of stimuli on the plate and on the cell to lead to the belief that there must be, physically, much in common between the actions in each case. *Prima facie* the formation of the normal latent image by

moderate light stimuli is parallel with the stimulation of growth by feeble X- or γ -radiation. The photographic reversal by greatly increased illumination compares with the inhibition of growth by the heavy doses of γ -radiation now employed in the treatment of cancer.

The analogy when further pursued must take account of intrinsic differences prevailing in the two cases. In the living cell there are continuous molecular movements and chemical interchanges accompanied by and attending the ionisation. The static conditions reached in the latent image can only prevail for a brief period which terminates when the ions and electrons find fresh combinations. The image-forming and reversing activities of the plate become respectively represented in the cell by the following events:— (a) Increased liberation of electrons (β -rays) and attendant formation of ions under the γ - or X-rays. This increases the metabolism, and, in the case of morbid growths, promotes the evil it is intended to cure. (b) With increasing radiation sudden and excessive electrostatic stress (or over-ionisation) brings about immediate reversion to the original molecular state so that molecular changes and reactions are stopped and metabolism ceases. The maintenance of this condition may lead to complete modification of the cell and ultimately to its absorption by the more stable normal cells which are not so readily influenced by the radiation. An alternative view, less in line with the photographic analogy, is to suppose that, with increased density of electronic radiation emanating from all parts of the tissues, an ion freshly formed in the metabolic substance of the cell is almost instantly neutralised by a β -ray, so that the time required for the molecular movements attending metabolism is not given and growth ceases.

In another particular we find the cell behaving in a similar manner to the photo-sensitive plate. Physicians ascribe the origin of malignant growth in certain cases to continued local irritation. Here we have a parallel with the photographic plate; for the latent image, *i.e.* the ionisation and electronisation of the film, may be obtained by various mechanical stimuli, such as pressure, friction, etc. The inhibition of the growth so produced in the tissues by γ -rays compares with the reversal of the pressure or friction marks of the film by light shock.

The selective action exhibited by the morbid cell towards the radiation, so that these cells are soonest affected by the rays, is significant. The therapeutic value of the rays depends on this action. To what may it be due?

Let us suppose the morbid cell characterised by less stable molecular systems than occur in the normal cell. In other words that the conditions obtaining in it are abnormally favourable to ionisation like a highly "ripened" photo-sensitive emulsion. A feeble radiation will accelerate the activity of

the morbid cell and yet scarcely affect the normal cell, the latter corresponding to a "slow" photo-sensitive film. Increased radiation which only attains the point of accelerating interchange in the normal cell may be attended by a sufficiently dense β -radiation to inhibit the metabolism in the morbid cell in the manner already suggested. In other words—to revert to the analogy with the photo-sensitive salt—the amount of ionic and electronic stimulus which builds the latent image in the "fast" film is insufficient to affect the "slow" film and as the stimulus is increased the latent image of the first suffers reversal at a point which builds up the latent image in the second. This appears to be just what is observed in the case of radiation treatment, the success of the method depending upon a lag in the effects arising in the normal tissues, as compared with those arising in the morbid tissues.

It may also be urged for the present view that if the effects of γ -rays on the growth of the cell are not of a photo-electric character, and so productive of ionisation, we must recognise in them some quite new reaction between matter and light. This seems a needless course when there does not appear to be any *a priori* objection to urge against the unification of our views respecting the photo-stimulation of the sensitive salt and the effects of γ -rays on the molecular systems existing in the cell.

Assuming a real basis for the approximation of the two processes, the question as to how the peculiar constitution of the morbid cell may arise deserves more careful consideration than I am competent to give to it. Upon the photographic analogy we might reason thus:—If, in the life of the cell, ions are naturally always being formed, the absence of a "restrainer" might lead to morbid ionisation; or, again, the presence of a "sensitiser"—the former to limit the ionising activity either physically by its inert properties, or chemically; the latter to accelerate it by removing the products of reaction as fast as they are formed. Dr. Lazarus-Barlow, however, has found notable and excessive quantities of radium in certain tumours. If this was general to all spontaneously arising cancers we might find here a sufficient cause of excessive ionisation. In this connection it is perhaps significant that the study of the distribution of cancer has been found to follow in a notable way the nature of the soil constituents of the district. Thus it is stated that cases of cancer are more frequent in clay-covered areas than in calcareous regions. Now calcareous rocks are almost without radioactive constituents, whether of the uranium-radium series or of the thorium series. The amounts of emanation continually being exhaled from such soils must be very different. It would be interesting to directly examine the several districts for soil-emanation.

Again, the well-known prevalence of cancer among chimney sweeps may be associated with the fact that charcoal and other forms of carbon, which must enter largely into the composition of soot, absorb radium emanation readily from the atmosphere. It is improbable that sweep-cancer is ascribable to skin irritation only, seeing that many other occupations (*e.g.* stone working, cement making) are exposed to even greater risks from that source.

On the theory that the cancer cell is the seat of excessive ionisation, we may ask if it is possible to control its activity. The latent image, although not possessed of the progressive fluxional characters of the cell, is, potentially, such an active configuration. It may be destroyed: (*a*) By such a light stimulus as will bring about reversal. The radioactive treatment of cancer is—on the present theory—an application of this fact. (*b*) By development, *i.e.* by such a chemical treatment as serves to discharge the ionised systems. The finding of a reagent which would act similarly on the morbid cell is, perhaps, not impossible. It would have to act selectively towards the less stable cell and must itself be ionised or become so in process of application. It would discharge the function of diverting the ionising activity to the formation of inert and harmless products.

In a sense we may regard development as continually progressing in the organic system, much as if a light-sensitive salt were maintained submerged in a developer while exposed to light. From this point of view it might be better to seek the intervention of a “restrainer” which would either retard molecular motions of diffusion, etc., in a mechanical way, *i.e.* by viscosity—as many restrainers are believed to do—or by chemically altering the nature of such conditions as result in growth and metabolism. If such remedies could be applied through the circulatory system, so as to reach metastases, depressing and lowering the abnormal ionic activity or directing its results into harmless channels, curative treatment might be attainable.

The theory here suggested for the processes going on in a cancer cell is a physical one, or, it may be said, takes account of the physical aspect primarily, and would involve the probability of successful treatment by experiments directed along physical and chemical lines. But it is not suggested that the origin of, or predisposition towards, abnormal ionic activity may not be founded in biologic causes. Nor does it enter into, or take account of, the probably extremely complex nature of the events progressing within the cell as leading to, or resulting from, the physical actions referred to in the theory.
